



SEQUENCE LISTING

<110> TORMO, MAR
TARI, ANA M.
LOPEZ-BERESTEIN, GABRIEL
MCDONNELL, TIMOTHY J.

<120> INHIBITION OF Bcl-2 PROTEIN EXPRESSION BY LIPOSOMAL
ANTISENSE OLIGODEOXYNUCLEOTIDES

<130> UTSC:550US

<140> 09/381,747
<141> 1999-09-23

<150> 08/726,211
<151> 1996-10-04

<160> 7

<170> PatentIn Ver. 2.1

<210> 1
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
Primer

<400> 1
cagcgtgcgc catccttc 18

<210> 2
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
Primer

<400> 2
acgtccgcc actccttccc 20

<210> 3
<211> 16
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
Primer

<400> 3
ctgaagggct tcttcc

16

<210> 4
<211> 5086
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1459) .. (2175)

<400> 4
gccccgccc ctccgcgccg cctgcccgcc cgcccgcgcg gctcccgcgc gccgctctcc 60
gtggccccgc cgcgctgccg ccgcccgcgc tgccagcgaa ggtgccgggg ctccggggccc 120
tccttgccgg cggcgcgtcag cgctcggagc gaactgcgcg acgggaggtc cgggaggcga 180
ccgtagtcgc gccgcccgcg aggaccagga ggaggagaaa ggggtgcgcg cccggaggcg 240
gggtgcgcgc gtgggggtgca gcggaagagg ggggccaggg gggagaactt cgtagcagtc 300
atccttttta ggaaaagagg gaaaaaataa aacctcccc caccacctcc ttctccccac 360
ccctgcgcgc accacacaca gcgcgggcct ctagcgctcg gcaccggcgg gccaggcgcg 420
tcctgccttc atttatccag cagcttttcg gaaaatgcat ttgctgttcg gagtttaatc 480
agaagacgat tcctgcctcc gtccccggtt ccttcacgtt cccatctccc ctgtctctct 540
cctggggagg cgtgaagcgg tcccgtggat agagattcat gcctgtgtcc gcgcgtgtgt 600
gcgcgcgtat aaattgccga gaaggggaaa acatcacagg acttctgcga ataccggact 660
gaaaattgta attcatctgc cgccgccgct gccaaaaaaa aactcgagct cttgagatct 720
ccggttgagg ttctgcgga ttgacatttc tgtgaagcag aagtctggga atcgatctgg 780
aaatcctcct aatttttact ccctctcccc ccgactcctg attcattggg aagtttcaaa 840
tcagctataa ctggagagtg ctgaagattg atgggacgtt tgcccttatgc atttgttttg 900
gttttacaaa aaggaaactt gacagaggat catgctgtac ttaaaaaata caagtaagtc 960
tcgcacagga aattgggtta atgtaacttt caatggaaac ctttgagatt ttttacttaa 1020
agtgcattcg agtaaattta atttocaggc agcttaatac attgttttta gccgtgttac 1080
ttgtagtgtg tatgcctgc tttcactcag tgtgtacagg gaaacgcacc tgatttttta 1140
cttattagtt tgttttttct ttaacctttc agcatcacag aggaagtaga ctgatattaa 1200
caatacttac taataataac gtgcctcatg aaataaagat ccgaaaggaa ttggaataaa 1260
aatttcctgc gtctcatgcc aagagggaaa caccagaatc aagtgttccg cgtgattgaa 1320

gacacccccct cgtccaagaa tgcaaagcac atccaataaa atagctggat tataactcct 1380
cttctttctc tgggggccgt ggggtgggag ctggggcgag aggtgccgtt ggcccccggt 1440
gcttttctc tgggaagg atg gcg cac gct ggg aga acg ggg tac gac aac 1491
Met Ala His Ala Gly Arg Thr Gly Tyr Asp Asn
1 5 10
cgg gag ata gtg atg aag tac atc cat tat aag ctg tcg cag agg ggc 1539
Arg Glu Ile Val Met Lys Tyr Ile His Tyr Lys Leu Ser Gln Arg Gly
15 20 25
tac gag tgg gat gcg gga gat gtg ggc gcc gcg ccc ccg ggg gcc gcc 1587
Tyr Glu Trp Asp Ala Gly Asp Val Gly Ala Ala Pro Pro Gly Ala Ala
30 35 40
ccc gca ccg ggc atc ttc tcc tcc cag ccc ggg cac acg ccc cat cca 1635
Pro Ala Pro Gly Ile Phe Ser Ser Gln Pro Gly His Thr Pro His Pro
45 50 55
gcc gca tcc cgc gac ccg gtc gcc agg acc tcg ccg ctg cag acc ccg 1683
Ala Ala Ser Arg Asp Pro Val Ala Arg Thr Ser Pro Leu Gln Thr Pro
60 65 70 75
gct gcc ccc ggc gcc gcc gcg ggg cct gcg ctc agc ccg gtg cca cct 1731
Ala Ala Pro Gly Ala Ala Ala Gly Pro Ala Leu Ser Pro Val Pro Pro
80 85 90
gtg gtc cac ctg gcc ctc cgc caa gcc ggc gac gac ttc tcc cgc cgc 1779
Val Val His Leu Ala Leu Arg Gln Ala Gly Asp Asp Phe Ser Arg Arg
95 100 105
tac cgc ggc gac ttc gcc gag atg tcc agc cag ctg cac ctg acg ccc 1827
Tyr Arg Gly Asp Phe Ala Glu Met Ser Ser Gln Leu His Leu Thr Pro
110 115 120
ttc acc gcg ccg gga cgc ttt gcc acg gtg gtg gag gag ctc ttc agg 1875
Phe Thr Ala Arg Gly Arg Phe Ala Thr Val Val Glu Glu Leu Phe Arg
125 130 135
gac ggg gtg aac tgg ggg agg att gtg gcc ttc ttt gag ttc ggt ggg 1923
Asp Gly Val Asn Trp Gly Arg Ile Val Ala Phe Phe Glu Phe Gly Gly
140 145 150 155
gtc atg tgt gtg gag agc gtc aac cgg gag atg tcg ccc ctg gtg gac 1971
Val Met Cys Val Glu Ser Val Asn Arg Glu Met Ser Pro Leu Val Asp
160 165 170
aac atc gcc ctg tgg atg act gag tac ctg aac cgg cac ctg cac acc 2019
Asn Ile Ala Leu Trp Met Thr Glu Tyr Leu Asn Arg His Leu His Thr
175 180 185
tgg atc cag gat aac gga ggc tgg gat gcc ttt gtg gaa ctg tac ggc 2067
Trp Ile Gln Asp Asn Gly Gly Trp Asp Ala Phe Val Glu Leu Tyr Gly
190 195 200

ccc agc atg cgg cct ctg ttt gat ttc tcc tgg ctg tct ctg aag act 2115
Pro Ser Met Arg Pro Leu Phe Asp Phe Ser Trp Leu Ser Leu Lys Thr
205 210 215

ctg ctc agt ttg gcc ctg gtg gga gct tgc atc acc ctg ggt gcc tat 2163
Leu Leu Ser Leu Ala Leu Val Gly Ala Cys Ile Thr Leu Gly Ala Tyr
220 225 230 235

ctg agc cac aag tgaagtcaac atgcctgccc caaacaata tgcaaaaggt 2215
Leu Ser His Lys

tcactaaagc agtagaaata atatgcattg tcagtgatgt accatgaaac aaagctgcag 2275
gctgtttaag aaaaaataac acacatataa acatcacaca cacagacaga cacacacaca 2335
cacaacaatt aacagtcttc aggcaaaacg tcgaatcagc tatttactgc caaagggaaa 2395
tatcatttat tttttacatt attaagaaaa aagatttatt tatttaagac agtcccatca 2455
aaactccgtc tttggaaatc cgaccactaa ttgccaaaca ccgcttcgtg tggctccacc 2515
tggatgttct gtgcctgtaa acatagattc gctttccatg ttgttggccg gatcaccatc 2575
tgaagagcag acggatggaa aaaggacctg atcattgggg aagctggctt tctggctgct 2635
ggaggctggg gagaaggtgt tcattcactt gcatttcttt gccctggggg cgtgatatta 2695
acagagggag ggttcccgtg gggggaagtc catgcctccc tggcctgaag aagagactct 2755
ttgcatatga ctacatgat gcatacctgg tgggaggaaa agagttggga acttcagatg 2815
gacctagtag cactgagat ttccacgccg aaggacagcg atgggaaaaa tgcccttaaa 2875
tcataggaaa gtatTTTTTTT aagctaccaa ttgtgccgag aaaagcattt tagcaattta 2935
tacaatatca tccagtacct taaaccctga ttgtgtatat tcatatattt tggatacgca 2995
ccccccaact cccaatactg gctctgtctg agtaagaaac agaatoctct ggaacttgag 3055
gaagtgaaca ttctgggtgac ttccgatcag gaaggctaga gttaccaga gcatcaggcc 3115
gccacaagtg cctgctttta ggagaccgaa gtccgcagaa cctacctgtg tcccagcttg 3175
gaggcctggt cctggaactg agccggggcc tctactggcct cctccaggga tgatcaacag 3235
ggtagtgtgg tctccgaatg tctggaagct gatggatgga gctcagaatt cactgtcaa 3295
gaaagagcag tagaggggtg tggctggggc tgtcaccctg gggccctcca ggtagggccg 3355
ttttcacgtg gagcatagga gccacgaccc ttcttaagac atgtatcact gtagagggaa 3415
ggaacagagg ccctgggcct tcctatcaga aggacatggg gaaggctggg aacgtgagga 3475
gaggcaatgg ccacggccca ttttggctgt agcacatggc acgttggctg tgtggccttg 3535
gccacctgtg agtttaaagc aaggctttaa atgactttgg agaggggtcac aaatcctaaa 3595

agaagcattg aagtgaggtg tcatggatta attgaccctt gtctatggaa ttacatgtaa 3655
 aacattatct tgtcactgta gtttggtttt atttgaaaac ctgacaaaaa aaaagttcca 3715
 ggtgtggaat atgggggtta tctgtacatc ctggggcatt aaaaaaaaaat caatggtggg 3775
 gaactataaa gaagtaacaa aagaagtgac atcttcagca aataaactag gaaatttttt 3835
 tttcttccag tttagaatca gccttgaaac attgatggaa taactctgtg gcattattgc 3895
 attatatacc atttatctgt attaactttg gaatgtactc tgttcaatgt ttaatgctgt 3955
 ggttgatatt tcgaaagctg ctttaaaaaa atacatgcat ctcagcgttt ttttgttttt 4015
 aattgtattt agttatggcc tatacactat ttgtgagcaa aggtgatcgt tttctgtttg 4075
 agatttttat ctcttgattc ttcaaaagca ttctgagaag gtgagataag ccctgagtct 4135
 cagctaccta agaaaaacct ggatgtcact ggccactgag gagctttggt tcaaccaagt 4195
 catgtgcatt tccacgtcaa cagaattggt tattgtgaca gttatatctg ttgtcccttt 4255
 gacctgtttt cttgaagggt tctctgtccc tgggcaatc cgcatttaat tcatggtatt 4315
 caggattaca tgcattgttg gttaaaccca tgagattcat tcagttaaaa atccagatgg 4375
 cgaatgacca gcagattcaa atctatggtg gtttgacctt tagagagttg ctttacgtgg 4435
 cctgtttcaa cacagaccca ccagagccc tctgcctc cttccgctgg ggctttctca 4495
 tggtgtcct tcagggctct cctgaaatgc agtggctgtt acgctccacc aagaaagcag 4555
 gaaacctgtg gtatgaagcc agacctccc ggcgggcctc agggacaga atgatcagac 4615
 ctttgaatga ttctaatttt taagcaaat attattttat gaaaggttta cattgtcaaa 4675
 gtgatgaata tggaatatcc aatcctgtgc tgcatactg ccaaatcat tttaatggag 4735
 tcagtttgca gtatgctcca cgtggtaaga tctccaagc tgcttttagaa gtaacaatga 4795
 agaacgtgga cgttttta ataaagcctg ttttgtcttt tgttggtgtt caaacgggat 4855
 tcacagagta tttgaaaaat gtatatatat taagaggtca cgggggctaa ttgctagctg 4915
 gctgcctttt gctgtgggtt tttgttacct ggttttaata acagtaaagtg tgcccagcct 4975
 cttggcccca gaactgtaca gtattgtggc tgcacttgct ctaagagtag ttgatgttgc 5035
 attttcttta ttgttaaaaa catgttagaa gcaatgaatg tatataaaag c 5086

<210> 5
 <211> 239
 <212> PRT
 <213> Homo sapiens

<400> 5

Met Ala His Ala Gly Arg Thr Gly Tyr Asp Asn Arg Glu Ile Val Met
 1 5 10 15
 Lys Tyr Ile His Tyr Lys Leu Ser Gln Arg Gly Tyr Glu Trp Asp Ala
 20 25 30
 Gly Asp Val Gly Ala Ala Pro Pro Gly Ala Ala Pro Ala Pro Gly Ile
 35 40 45
 Phe Ser Ser Gln Pro Gly His Thr Pro His Pro Ala Ala Ser Arg Asp
 50 55 60
 Pro Val Ala Arg Thr Ser Pro Leu Gln Thr Pro Ala Ala Pro Gly Ala
 65 70 75 80
 Ala Ala Gly Pro Ala Leu Ser Pro Val Pro Pro Val Val His Leu Ala
 85 90 95
 Leu Arg Gln Ala Gly Asp Asp Phe Ser Arg Arg Tyr Arg Gly Asp Phe
 100 105 110
 Ala Glu Met Ser Ser Gln Leu His Leu Thr Pro Phe Thr Ala Arg Gly
 115 120 125
 Arg Phe Ala Thr Val Val Glu Glu Leu Phe Arg Asp Gly Val Asn Trp
 130 135 140
 Gly Arg Ile Val Ala Phe Phe Glu Phe Gly Gly Val Met Cys Val Glu
 145 150 155 160
 Ser Val Asn Arg Glu Met Ser Pro Leu Val Asp Asn Ile Ala Leu Trp
 165 170 175
 Met Thr Glu Tyr Leu Asn Arg His Leu His Thr Trp Ile Gln Asp Asn
 180 185 190
 Gly Gly Trp Asp Ala Phe Val Glu Leu Tyr Gly Pro Ser Met Arg Pro
 195 200 205
 Leu Phe Asp Phe Ser Trp Leu Ser Leu Lys Thr Leu Leu Ser Leu Ala
 210 215 220
 Leu Val Gly Ala Cys Ile Thr Leu Gly Ala Tyr Leu Ser His Lys
 225 230 235

<210> 6
 <211> 911
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (147)..(761)

<400> 6

tgattgaaga	cacccccctcg	tccaagaatg	caaagcacat	ccaataaaaat	agctggatta	60										
taactcctct	tctttctctg	ggggccgtgg	ggtgggagct	ggggcgagag	gtgccgttgg	120										
cccccgttgc	ttttcctctg	ggaagg	atg	gcg	cac	gct	ggg	aga	acg	ggg	tac	173				
			Met	Ala	His	Ala	Gly	Arg	Thr	Gly	Tyr					
			1				5									
gac	aac	cgg	gag	ata	gtg	atg	aag	tac	atc	cat	tat	aag	ctg	tcg	cag	221
Asp	Asn	Arg	Glu	Ile	Val	Met	Lys	Tyr	Ile	His	Tyr	Lys	Leu	Ser	Gln	
10					15					20					25	
agg	ggc	tac	gag	tgg	gat	gcg	gga	gat	gtg	ggc	gcc	gcg	ccc	ccg	ggg	269
Arg	Gly	Tyr	Glu	Trp	Asp	Ala	Gly	Asp	Val	Gly	Ala	Ala	Pro	Pro	Gly	
				30					35					40		
gcc	gcc	ccc	gca	ccg	ggc	atc	ttc	tcc	tcc	cag	ccc	ggg	cac	acg	ccc	317
Ala	Ala	Pro	Ala	Pro	Gly	Ile	Phe	Ser	Ser	Gln	Pro	Gly	His	Thr	Pro	
			45					50					55			
cat	cca	gcc	gca	tcc	cgc	gac	ccg	gtc	gcc	agg	acc	tcg	ccg	ctg	cag	365
His	Pro	Ala	Ala	Ser	Arg	Asp	Pro	Val	Ala	Arg	Thr	Ser	Pro	Leu	Gln	
		60					65					70				
acc	ccg	gct	gcc	ccc	ggc	gcc	gcc	gcg	ggg	cct	gcg	ctc	agc	ccg	gtg	413
Thr	Pro	Ala	Ala	Pro	Gly	Ala	Ala	Ala	Gly	Pro	Ala	Leu	Ser	Pro	Val	
	75					80					85					
cca	cct	gtg	gtc	cac	ctg	gcc	ctc	cgc	caa	gcc	ggc	gac	gac	ttc	tcc	461
Pro	Pro	Val	Val	His	Leu	Ala	Leu	Arg	Gln	Ala	Gly	Asp	Asp	Phe	Ser	
90					95					100					105	
cgc	cgc	tac	cgc	ggc	gac	ttc	gcc	gag	atg	tcc	agc	cag	ctg	cac	ctg	509
Arg	Arg	Tyr	Arg	Gly	Asp	Phe	Ala	Glu	Met	Ser	Ser	Gln	Leu	His	Leu	
				110					115					120		
acg	ccc	ttc	acc	gcg	cgg	gga	cgc	ttt	gcc	acg	gtg	gtg	gag	gag	ctc	557
Thr	Pro	Phe	Thr	Ala	Arg	Gly	Arg	Phe	Ala	Thr	Val	Val	Glu	Glu	Leu	
			125					130					135			
ttc	agg	gac	ggg	gtg	aac	tgg	ggg	agg	att	gtg	gcc	ttc	ttt	gag	ttc	605
Phe	Arg	Asp	Gly	Val	Asn	Trp	Gly	Arg	Ile	Val	Ala	Phe	Phe	Glu	Phe	
		140					145					150				
ggt	ggg	gtc	atg	tgt	gtg	gag	agc	gtc	aac	cgg	gag	atg	tcg	ccc	ctg	653
Gly	Gly	Val	Met	Cys	Val	Glu	Ser	Val	Asn	Arg	Glu	Met	Ser	Pro	Leu	
	155					160					165					
gtg	gac	aac	atc	gcc	ctg	tgg	atg	act	gag	tac	ctg	aac	cgg	cac	ctg	701
Val	Asp	Asn	Ile	Ala	Leu	Trp	Met	Thr	Glu	Tyr	Leu	Asn	Arg	His	Leu	
170					175					180					185	
cac	acc	tgg	atc	cag	gat	aac	gga	ggc	tgg	gta	ggt	gca	tct	ggt	gat	749
His	Thr	Trp	Ile	Gln	Asp	Asn	Gly	Gly	Trp	Val	Gly	Ala	Ser	Gly	Asp	
				190					195					200		
gtg																

Val Ser Leu Gly
205

ggctcctggg caatgggagg ctgtggagcc ggcgaaataa aatcagagtt gttgcttccc 861

ggcgtgtccc tacctcctcc tctggacaaa gcgttcactc ccaacctgac 911

<210> 7

<211> 205

<212> PRT

<213> Homo sapiens

<400> 7

Met Ala His Ala Gly Arg Thr Gly Tyr Asp Asn Arg Glu Ile Val Met
1 5 10 15

Lys Tyr Ile His Tyr Lys Leu Ser Gln Arg Gly Tyr Glu Trp Asp Ala
20 25 30

Gly Asp Val Gly Ala Ala Pro Pro Gly Ala Ala Pro Ala Pro Gly Ile
35 40 45

Phe Ser Ser Gln Pro Gly His Thr Pro His Pro Ala Ala Ser Arg Asp
50 55 60

Pro Val Ala Arg Thr Ser Pro Leu Gln Thr Pro Ala Ala Pro Gly Ala
65 70 75 80

Ala Ala Gly Pro Ala Leu Ser Pro Val Pro Pro Val Val His Leu Ala
85 90 95

Leu Arg Gln Ala Gly Asp Asp Phe Ser Arg Arg Tyr Arg Gly Asp Phe
100 105 110

Ala Glu Met Ser Ser Gln Leu His Leu Thr Pro Phe Thr Ala Arg Gly
115 120 125

Arg Phe Ala Thr Val Val Glu Glu Leu Phe Arg Asp Gly Val Asn Trp
130 135 140

Gly Arg Ile Val Ala Phe Phe Glu Phe Gly Gly Val Met Cys Val Glu
145 150 155 160

Ser Val Asn Arg Glu Met Ser Pro Leu Val Asp Asn Ile Ala Leu Trp
165 170 175

Met Thr Glu Tyr Leu Asn Arg His Leu His Thr Trp Ile Gln Asp Asn
180 185 190

Gly Gly Trp Val Gly Ala Ser Gly Asp Val Ser Leu Gly
195 200 205